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14. ABSTRACT

We show that laser-driven thermal modification can be used to selectively enhance regions of a flowing carbon suspension. The preliminary proof-of-principle experiments illustrate the ability to measure thermal modifications in a time-resolved manner utilizing x-ray phase-contrast imaging paving the way for implementation in a biological model. Additional results of biological tissue sample measurements are presented. X-ray phase-contrast images of murine hepatic and pulmonary samples reveal fine structure usually visible only by utilizing histological or microscopy techniques. The method holds promise for future applications to study murine models of pulmonary and hepatic disease.

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Introduction

Thermally Modulated X-ray Phase Contrast Imaging

The experimental setup for modifying a phase contrast x-ray image by using laser-driven thermal gradients is illustrated in Figure 1. The output of a 527nm Nd:YLF laser is focused onto a liquid water jet of carbon suspension and imaged using a microfocus x-ray source coupled in-line with a synchronously gated intensified optically coupled CCD camera.

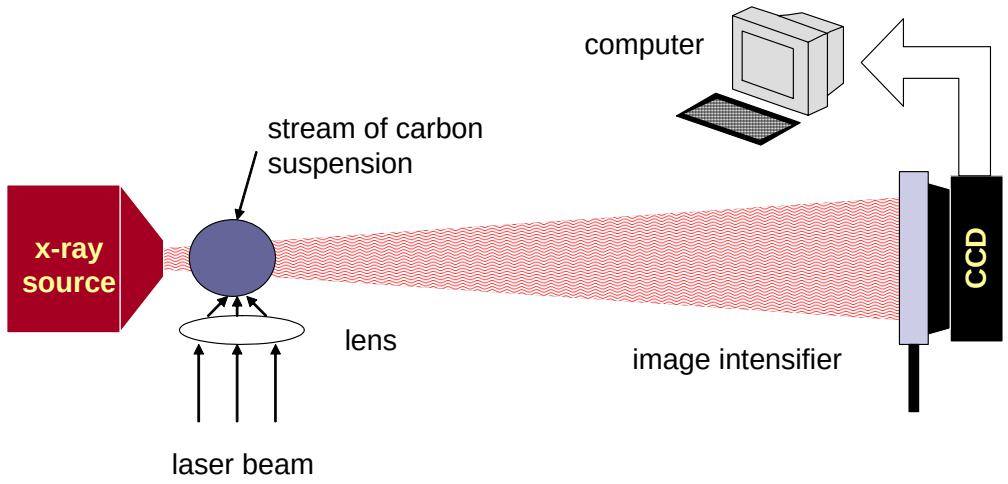

Figure 1 : Diagram of the experimental apparatus. X-radiation generated by a microfocus tube penetrates a sample irradiated by a the focused output of 527nm Nd:YAG laser. A gated intensified optically coupled CCD camera detects the transmitted x-rays and is read by the computer that stores the images.

In principle, the sensitivity of x-ray phase-contrast imaging allows the visualization of weak phase effects imparted to x-ray photons as they traverse a thermally modulated sample. Biologically, these experiments hold promise to take advantage of the rather large optical contrast of blood in the infrared to modulate x-ray images. By using a liquid jet of carbon suspension we experimentally investigate the basic principles of laser modulated x-ray phase-contrast imaging.

In addition to image modulation, the need to develop biological sample preparation methods designed to take advantage the proliferation of high-resolution x-ray sources. The goal of the current research is to explore the uses of phase-contrast x-ray imaging for investigating both static and laser-modulated biological samples.

Body

The right-hand image in Figure 2 shows the results of a set of experiments involving the interaction of a focused laser with a flowing carbon suspension in water. The figure on the left illustrates an x-ray image of the jet without laser modification. The features labeled a, b and c in Figure 2 shows the modification of the jet induced by the laser-driven thermal heating. Each of the three features arises from thermal jet expansion

caused by the interaction of subsequent laser pulses. The result has two-fold importance: First, the thermal gradient is clearly visible in the x-ray absorption image and, second, the principle of acquiring time-resolved x-ray images is demonstrated.

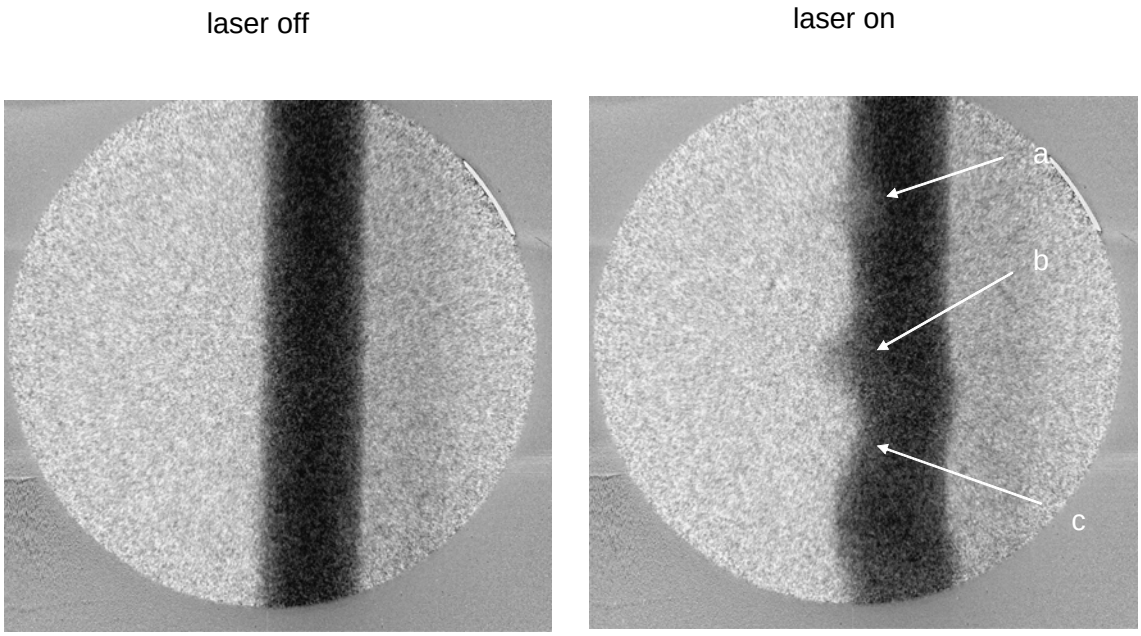

Figure 2. (Left) An X-ray image of a flowing stream of an aqueous carbon suspension. (Right) X-ray image of the carbon suspension synchronized with the firing of the laser. The point marked (a) corresponds to the position where the laser beam is focused.

We have also tested the ability of x-ray phase-contrast imaging technique to image microvasculature in mouse liver samples given to us by our collaborators at Brown University Medical School. Figure 3 shows a typical x-ray phase-contrast image of an excised, formaldehyde-fixed and dried murine liver sample. The images reveal highly resolved structure attributed to the presence of air-filled venous vessels and micro-vessels. The preparation technique takes advantage of the permeable physical properties of the liver to promote air filling of the vessels when dried. The large difference in the x-ray index of refraction for air versus soft tissue gives rise to sharp phase-contrast features in the x-ray images. Going forward, this imaging method coupled with the preparation technique will be implemented to visualize neovascularization associated with tumor proliferation in a murine model of hepatocellular carcinoma.

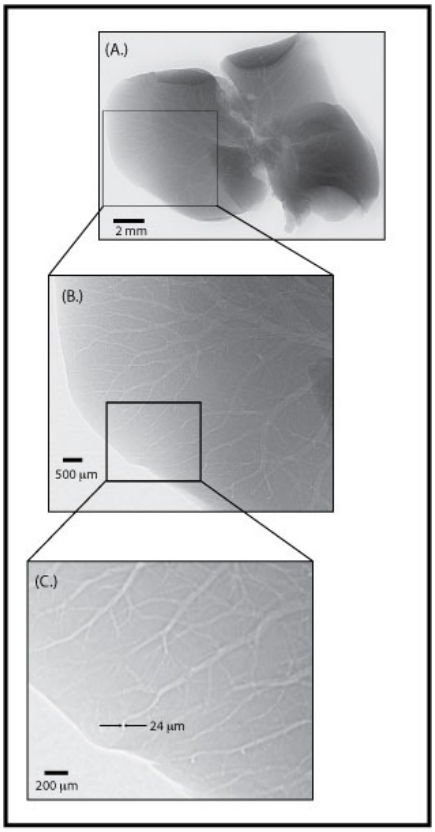

Figure 3. X-ray phase contrast image of a formaldehyde-fixed and dried mouse liver sample. Microvessels are resolved to their finest levels.

Given the inherent advantages of having air and soft-tissue interfaces for x-ray phase-contrast imaging, murine pulmonary samples were also imaged. Figure 3 displays a typical result of an excised rat lung, which has been clamped and partially inflated with air. Alveolar features down to 10 μm are visible. The speckled pattern is indicative of air and soft-tissue interfaces expected with the inflation of the alveolar sacs. Also visible are darker web-like features, attributed to pulmonary venous vasculature. The ability to image pulmonary samples with this type of detail naturally lends itself to the study of pulmonary pathologies. For example, utilizing the imaging technique to image murine models of pulmonary fibrosis, emphysema, and cancer could provide valuable access to fine structure usually attained only by histological methods.

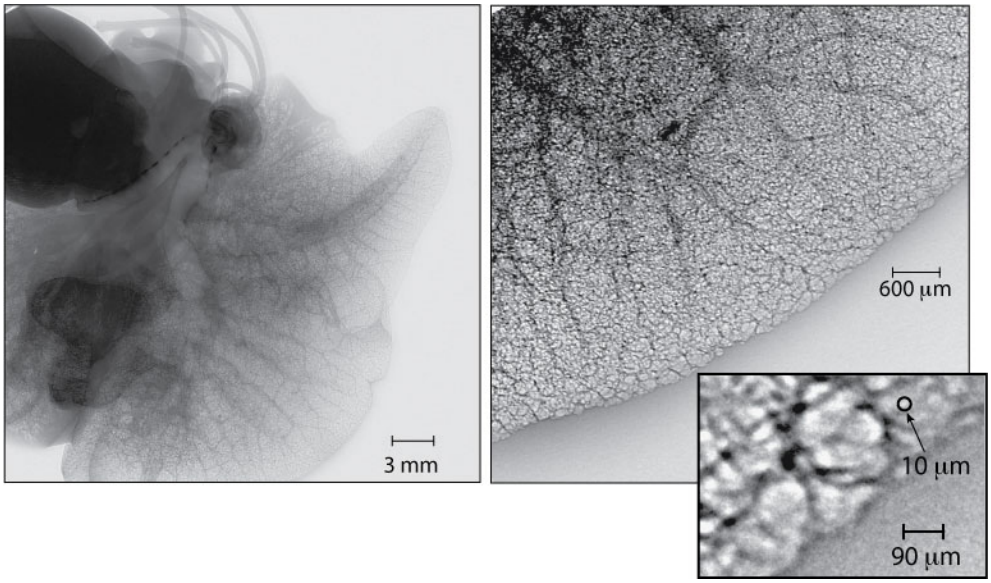

Figure 4 Three magnified views of a phase contrast image of an air-filled excised rat lung.

Reportable Outcomes

"High-resolution angiography: Computed tomography coupled X-ray phase contrast imaging of biological tissue samples" with C. M. Laperle, T. J. Hamilton, P. Wintermeyer, D. Shi, M. Anastasio, C. Rose-Petruck, G. and J. R. Wands ***in preparation***

C. M. Laperle, G. Cao, T. J. Hamilton, C. Rose-Petruck, and G. J. Diebold, "Photothermal Modification of X-ray Phase Contrast Images", ***Progress in Biomedical Optics and Imaging, Photons Plus Ultrasound: Imaging and Sensing 2007***, 8 64371N, (2007).

"X-ray Phase Contrast Imaging: Transmission Functions Separable in Cartesian Coordinates", with Guohua Cao, Theron Hamilton, Christopher Laperle and Christoph Rose-Petruck ***submitted to Journal of the Optical Society of America A.***

Conclusions

We have proven the concept of laser-driven thermally modified x-ray phase contrast imaging. We have shown the method has the ability to visualize thermally modified regions of objects. Furthermore, we have shown the sensitivity of phase-contrast x-ray imaging on excised hepatic and pulmonary murine tissue samples.

References

1. Born, M. & Wolf, E. *Principles of Optics* (ed. Press, P.) (Pergamon Press, Oxford, England, 1980).
2. Cowley, J. M. (ed.) *Electron Diffraction* (Kluwer Academic Publishers, Dordrecht, 1991).
3. Cowley, J. M. *Diffraction Physics* (North Holland Physics Publishing, a division of Elsevier Science Publishers B.V., Amsterdam, 1984).
4. A Snigirev, I. S., V Kohn, S Kuznetsov, I Schelokov. On The Possibility of X-ray Phase Contrast Microimaging by Coherent High-energy Synchrotron Radiation. *Rev. Sci. Instr.* **66**, 5486 (1995).
5. Fulvia Arfelli, V. B., Alberto Bravin, Giovanni Cantatore, Edoardo Castelli et al. Mammography with Synchrotron Radiation: Phase Detection Techniques. *Radiology* **215**, 286-293 (2000).
6. Momose, A. Demonstration of phase-contrast x-ray computed tomography using an x-ray interferometer. *Nuclear Instruments & Methods in Physics Research, Section A: Accelerators, Spectrometers, Detectors, and Associated Equipment* **352**, 622-8 (1995).
7. Pogany, A., Gao, D. & Wilkins, S. W. Contrast and resolution in imaging with microfocus x-ray source. *Rev. Sci. Instr.* **68**, 2774 (1997).
8. Krol, A. et al. Laser-based microfocused x-ray source for mammography: Feasibility study. *Medical Physics* **24**, 725-732 (1997).
9. Krol, A., Kieffer, J. C. & Forster, E. Laser-driven x-ray source for diagnostic radiology. *Proceedings of SPIE-The International Society for Optical Engineering* **3157**, 156-163 (1997).
10. Beckmann, F., Bonse, U., Busch, F. & Gunnewig, O. X-ray microtomography (microCT) using phase contrast for the investigation of organic matter. *Journal of Computer Assisted Tomography* **21**, 539-53 (1997).
11. Westervelt, P. The Theory of steady Forces Caused by Sound Waves. *J. Acoust. Soc. Am.* **23**, 312 (1951).
12. Morse, P. M. *Vibration and Sound* (ed. Physics, A. I. o.) (Acoustical Society of America, 1981).
13. Muthupillai, R. et al. Magnetic resonance elastography by direct visualization of propagating acoustic strain waves. *Science (Washington, D. C.)* **269**, 1854-7 (1995).
14. Gao, L., Parker, K. J., Lerner, R. M. & Levinson, S. F. Imaging of the elastic properties of tissue--a review. *Ultrasound in Medicine and Biology* **22**, 959-77 (1996).
15. Fatemi, M. & Greenleaf, J. F. Ultrasound-stimulated vibro-acoustic spectrography. *Science* **280**, 82-5 (1998).
16. Nightingale, K., Nightingale, R., Palmeri, M. & Trahey, G. in *IEEE Ultrasonics Symp* 1319 (1999).
17. Sarvazyan, A. P. Shear Wave Elasticity Imaging: A New Ultrasonic Technology of Medical Diagnostics. *Ultrasound in Medicine and Biology* **24**, 1419 (1998).
18. McAleavey, S. A. Estimates of Echo Correlation and Measurement Bias in Acoustic Radiation Force Impulse Imaging. *IEEE Transactions on Ultrasonics, Ferroelectrics and Frequency Control* **50**, 631 (2003).

19. Nightingale, K., Stutz, D., Bentley, R. & Trahey, G. in *IEEE Symp* 525 (2002).
20. King, L. V. On the Acoustic Radiation Pressure on Spheres. *Proceedings of the Royal Society of London, Series A, Mathematical and Physical Sciences* **147**, 212-240 (1934).
21. C. J. Bailat, T. Hamilton, Rose-Petruck, C. & Diebold, G. J. Acoustic radiation pressure: a phase contrast agent for x-ray phase contrast imaging. *Appl. Phys. Lett.* **85**, 4517-4519 (2004).
22. T. Hamilton, C. J. Bailat, Rose-Petruck, C. & Diebold, G. J. Acoustically Modulated X-ray Phase Contrast Imaging. *Phys Med Biol* **49**, 4985-4996 (2004).
23. Wilkins, S. W., Gureyev, T. E., Gao, D., Pogany, A. & Stevenson, A. W. Phase-contrast imaging using polychromatic hard x-rays. *Nature* **384**, 335-338 (1996).
24. Radon, J. Über die Bestimmung von Funktionen durch Integralwerte längs gewisser Mannigfaltigkeiten, Berichte Sächsische Akademie der Wissenschaften. *Math.-Phys. Kl.* **69**, 262-267 (1917).